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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/680,356	10/06/2003	Chiaki Ishii	58600-8229.US00	5651

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EXAMINER	
POPA, ILEANA	
ART UNIT	PAPER NUMBER
1633	
MAIL DATE	DELIVERY MODE
04/27/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/680,356	ISHII ET AL.	
	Examiner	Art Unit	
	ILEANA POPA	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 January 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-4, 6-18, and 21* is/are pending in the application.

4a) Of the above claim(s) *13-18 and 21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 6-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. In view of Panel Decision from the Pre-Appeal Brief conference held on 02/25/2010, PROSECUTION IS REOPENED and a new Office action is hereby issued to make the full Niemeyer (DE 19902391) reference of record.

Claims 5, 19, and 20 have been cancelled. Claims 13-18 and 21 have been withdrawn.

Claims 1-4 and 6-12 are under examination.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 1-4, 6, 7, 9, 11, and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boxer et al. (WO98/23948, of record), in view of both Boukobza et al. (J Phys Chem, 2001, 105: 12165-12170, of record) and Niemeyer et al. (DE 19902391).

Boxer et al. teach a surface detector array device comprising a substrate defining a plurality of distinct bilayer-compatible surface regions separated by one or more bilayer barrier regions, a bulk aqueous phase covering the substrate surface, a lipid bilayer expanse carried on each of the bilayer-compatible region, and an aqueous film

interposed between each bilayer-compatible region and the corresponding lipid bilayer expanse, i.e., the aqueous film is interposed between the bilayer-compatible surface region and the lower surface of the corresponding bilayer expanse (claims 1 and 9) (p. 4, lines 5-12). Boxer et al. teach that the bilayer expanses may be modified so that they comprise lipids covalently coupled to biomolecules wherein each bilayer expanse could have a specific biomolecule and wherein the biomolecules can be non-covalently attached to the bilayer via specific molecular interactions such as biotin/avidin interactions (claim 1) (p. 4, line 32 through p. 5, line 5). Therefore, Boxer et al. teach that the lipid bilayer expanses have different compositions (claim 3). With respect to the limitation of inner and outer surfaces (claim 1), a bilayer lipid necessarily has inner and outer surfaces; therefore, Boxer et al. do teach lipid bilayer expanses with an inner and an outer bilayer surface (compare also Fig. 1 of the international publication WO98/23948 with Fig. 1 of the instant application, both depicting the same composition). Boxer et al. teach that the bilayers could comprise lipids covalently coupled to polynucleotides (p. 16, lines 3-21). The bilayer-compatible surface regions may be formed of materials such as SiO_2, MgF_2, CaF_2, and mica (claim 11) and the bilayer expanse may comprise phosphatidylcholine (claim 12) (p. 4, lines 13-15 and 20-24). Boxer et al. also teach that one embodiment relates to sorting devices for biomolecules integrated or attached to the supported bilayer, wherein the device comprises barrier regions acting as two dimensional sieves having progressively smaller openings that are capable to sort the membrane-associated molecule by size,

i.e., the array comprises discrete bilayer patches associated with the lipid bilayer expanses (claim 2) (p. 25 bridging p. 26 and Fig. 5).

Boxer et al. do not teach the biomolecule being a vesicle or second biomolecules associated with the bilayer expanses wherein the second biomolecules are capable of freely moving within the expanse, nor do they teach some of the bilayer expanses as having different second molecules (claims 1, 6, and 7). However, using such is suggested by the prior art. For example, Boukobza et al. teach a novel immobilization technique for biomolecules comprising trapping single protein molecules inside lipid vesicles (i.e., a first and a second biomolecule), which are tethered to a supported lipid bilayer via biotin-avidin interactions, wherein the technique overcomes the problem of molecule-surface interaction and wherein the surface-tethered vesicles can be used for experiments on reconstituted membrane proteins and peptides (i.e., a vesicle capable of specifically binding a test agent) (claims 1 and 6) (p. 12165, column 2, second paragraph, p. 12166, column 1, Fig. 1, p. 12169, column 2, *Conclusion*). Based on these teachings, one of skill in the art would have known that the array of supported bilayers of Boxer et al. is also suitable for vesicles tethering. It would have been obvious to one of skill in the art, at the time the invention was made, to modify the array of Boxer et al. by tethering vesicles via biotin/avidin interactions to achieve the predictable result of obtaining an array suitable for experiments on reconstituted membrane proteins and peptides.

Boxer et al. and Boukobza et al. teach tethering via biotin/avidin interactions and not via oligonucleotide hybridization (claim 1). However, doing such is suggested by the

prior art. For example, Niemeyer et al. teach that tethering via oligonucleotide hybridization offers advantages over the other tethering means such as biotin/avidin interactions in that: **(i)** it permits the efficient and simultaneous immobilization of many different macromolecules in a single reaction step at specific places on the substrate; and **(ii)** it allows the regeneration of the substrate for multiple uses (p. 3; p. 4, first full paragraph; Example 1). Niemeyer et al. teach that the macromolecules could be vesicles (p. 8, first paragraph). It would have been obvious to one of skill in the art, at the time the invention was made, to modify the array of supported bilayers of Boxer et al. and Boukobza et al. by tethering their vesicles via oligonucleotide hybridization, with a reasonable expectation of success. One of skill in the art would have been motivated to do such in order to obtain reusable expanses with different vesicle composition, each vesicle being encoded by a specific oligonucleotide, as needed. One of skill in the art would have been expected to have a reasonable expectation of success in doing so because Boxer et al. teaches that lipids covalently coupled to nucleic acids (i.e., oligonucleotides) can be easily incorporated into the lipid bilayers and because Niemeyer et al. teach that oligonucleotides incorporated into supports can be successfully used to tether to the supports macromolecules functionalized with the complementary oligonucleotides.

With respect to the limitation recited in claim 6, absent evidence to the contrary, the protein-loaded vesicles are able to freely move within the expanse. With respect to the limitation recited in claim 7, one of skill in the art would have been motivated to use

different second molecules in order to study the reconstitution of several membrane proteins at the same time.

Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

4. Claims 1-4, 6, 7, and 9-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boxer et al. taken with both Boukobza et al. and Niemeyer et al., in further view of each Cornell et al. (U.S. Patent No. 5, 874,316, of record), Arnold et al. (U.S. Patent 5, 310, 648, of record), and Bayerl et al. (U.S. Patent No. 6,051,372, of record).

The teachings of Boxer et al., Boukobza et al., and Niemeyer et al. are applied as above for claims 1-4, 6, 7, 9, 11, and 12.

Boxer et al., Boukobza et al., and Niemeyer et al. do not teach the use of self-limiting lateral diffusion to separate the lipid regions from one another (claim 10). However, at the time the invention was made, self-limiting lateral diffusion to separate the lipid regions from one another was taught by the prior art. For example, Cornell et al. teach receptor membranes, wherein the monomers in the membrane may be prevented from diffusing laterally by selecting lipids that are crystalline at room temperature, which eliminates lateral diffusion (column 3, lines 25-29). Arnold et al. teach an imprinted matrix, wherein the spatial organization of molecules in the substrate can be locked into place by a variety of means to form a structure incapable of lateral diffusion, for example by decreasing fluidity (column 7, lines 11-24, column 8, lines 1-

10). Bayerl et al. teach patterned surfaces, wherein the lateral diffusion can be prevented by switching the lipid bilayer phase to gel or crystalline and wherein the phase transition can be accomplished by adjusting one physical parameter, the temperature (column 4, lines 25-58, column 5, lines 4-25, column 7, lines 1-24, column 9, lines 32-53). It would have been obvious to one of skill in the art, at the time the indention was made, to maintain the substrate orientation by limiting the lateral diffusion as taught by Cornell et al., Arnold et al., or Bayerl et al., with a reasonable expectation of success. One of skill in the art would have been motivated to do so because the prior art teaches that the use of self-limiting lateral diffusion to keep the lipid regions apart obviates the need for physical barriers on the substrate surface. One of skill in the art would have been expected to have a reasonable expectation of success in using any of the above-mentioned techniques because the art teaches the successful use of such techniques to limit lateral diffusion between discrete lipid regions.

Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

5. Claims 1-4, 6-9, 11, and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boxer et al. taken with both Boukobza et al. and Niemeyer et al., in further view of Shen et al. (PGPUB 2003/0148335, of record).

The teachings of Boxer et al., Boukobza et al., and Niemeyer et al. are applied as above for claims 1-4, 6, 7, 9, 11, and 12.

Boxer et al., Boukobza et al., and Niemeyer et al. do not teach the identity of the

biomolecule being determined from the sequence of the oligonucleotide (claim 8). Shen et al. teach the use of oligonucleotide identification tags for assaying the identity of non-nucleic acid targets, wherein the method can be used to identify any non-nucleic acid target associated with any surface (Abstract, p. 2, paragraphs 0009 and 0012, p. 3, paragraph 0017). Shen et al. teach that the oligonucleotide tag can be identified without dissociation by hybridization analysis, wherein the tag is detected by contacting it with an array of complementary nucleic acids immobilized on a support (p. 3, paragraphs 0021 and 0023). Therefore, it would have been obvious to one of skill in the art, at the time the invention was made, to determine the identity of the biomolecule from hybridization analysis of its attached oligonucleotide with the complementary oligonucleotide present on the bilayer expanse, as taught by Shen et al. with a reasonable expectation of success. One of skill in the art would have been expected to have a reasonable expectation of success in using such a method because the art teaches the successful use of oligonucleotide hybridization in determining the identity of oligonucleotide-tagged biomolecules.

Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

6. No claim is allowed. No claim is free of prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ILEANA POPA whose telephone number is (571)272-5546. The examiner can normally be reached on 9:00 am-5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ileana Popa/
Primary Examiner, Art Unit 1633